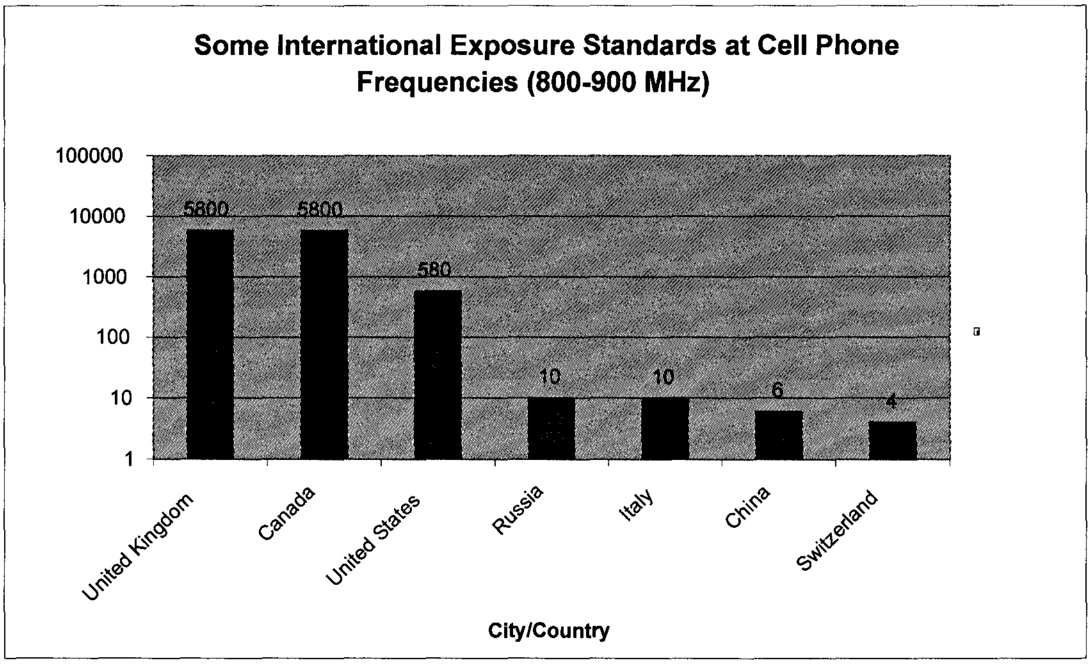
Table 3.3 Some International Exposure Standards at Cell Phone Frequencies



Professional bodies from technical societies like IEEE and ICNIRP continue to support "thermal-only" guidelines routinely defend doing so a) by omitting or ignoring study results reporting bioeffects and adverse impacts to health and wellbeing from a very large body of peer-reviewed, published science because it is not yet "proof" according to their definitions; b) by defining the proof of "adverse effects" at an impossibly high a bar (scientific proof or causal evidence) so as to freeze action; c) by requiring a conclusive demonstration of both "adverse effect" and risk before admitting low-intensity effects should be taken into account; e) by ignoring low-intensity studies that report bioeffects and health impacts due to modulation; f) by conducting scientific reviews with panels heavily burdened with industry experts and under-represented by public health experts and independent scientists with relevant low-intensity research experience; g) by limiting public participation in standard-setting deliberations; and other techniques that maintain the status quo.

Much of the criticism of the existing standard-setting bodies comes because their contributions are perceived as industry-friendly (more aligned with technology investment and dissemination of new technologies) rather than public health oriented. The view of the Chair of the latest IEEE standard-setting ICES Eleanor Adair is made clear by Osepchuk and Petersen (2003) who write in the abstract of their paper "*her goal and the goal of ICES is to establish rational standards that will make future beneficial applications of RF energy credible to humanity.*" Authors Osepchuk and Petersen note that *"(I)t is important that safety standards be rational and avoid excessive safety margins."* The authors specifically dismiss the body of evidence for low-intensity effects with *"(A)lthough the literature reporting "athermal" bioeffects of exposure to* *microwave/RF energy (other than electrostimulation) is included in the review process, it has been found to be inconsistent and not useful for purposes of standard-setting."*

This report addresses the substantial body of evidence reporting low-intensity effects from electromagnetic fields (both power-frequency fields in the ELF range, and radiofrequency/microwave fields at exposure levels that do not involve any heating. It also addresses the inconsistency in the literature quoted as the basis for retaining thermal-only exposure standards (see particularly the Genotoxics Section 6 where half of more of the published papers report negative effects and half positive effects).

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Osepchuk JM Petersen RC. 2003. Historical Review of RF Exposure Standards and the International Committee on Electromagnetic Safety (ICES). Bioelectromagnetics Supplement 6:S7-16. Osepchuk is a former employee of Raytheon. Petersen is a former employee of Bell Labs and Lucent Technologies. Both are independent industry consultants in their retirement.

SECTION 4: EVIDENCE FOR INADEQUACY OF THE STANDARDS

Evidence for judging the adequacy (or inadequacy) of the existing ICNIRP and IEEE C95.1 radiofrequency radiation standards can be taken from many relevant sources. The ICNIRP standards are similar to the IEEE (except for the new C95.1 -2006) revisions by IEEE SC-4), and these discussions can be used to evaluate both sets of public exposure standards for adequacy (or inadequacy).

An important screen for assessment of how review bodies conduct their science reviews and resulting conclusions on the adequacy of ELF and RF exposure limits depends on embedded assumptions. The singularly most important embedded assumption is whether these bodies assume from the beginning that only conclusive scientific evidence (proof) will be sufficient to warrant change; or whether actions should be taken on the basis of a growing body of evidence which provides early but consequential warning of (but not yet proof) of possible risks.

As a result of current international research and scientific discussion on whether the prevailing RF and ELF standards are adequate for protection of public health, there are many recent developments to provide valuable background on the uncertainty about whether current standards adequately protect the public.

World Health Organization Draft Framework for Electromagnetic Fields

The International EMF Project was established by WHO in 1996. Its mission was to *"pool resources and knowledge concerning the effects of exposure to EMF and make a concerted effort to identify gaps in knowledge, recommend focused research programmes that allow better health risk assessments to be made, conduct updated critical reviews of the scientific literature, and work towards an international consensus and solutions on the health concerns."* (WHO September 1996 Press Release - Welcome to the International EMF Project)

The stated role of the WHO Precautionary Framework on EMF Health Risk Research (Radiation and Environment Health) has termed its objectives as follows;

- to anticipate and respond to possible threats before introduction of an agent or technology
- to address public concerns that an uncertain health risk is minimized after introduction of an agent
- to develop and select options proportional to the degree of scientific certainty, the severity of harm, the size and nature of the affected population and the cost.

The role of WHO is advisory only to the countries of Europe but it is an important function and can significantly affect decision-making on public health issues. It provides analysis and recommendations on various topics of health and environment, for consideration by member countries of the EU. Given the EU Article 174 policy requires a precautionary approach to judging health and environmental risks, and given that the charter of WHO is to serve the needs of the EU, one would think it essential that the WHO EMF Program health criteria results should be guided by and tailored to compliance with Article 174. This needs to occur in the assessment of the scientific literature (e.g., not requiring studies to provide scientific proof or causal scientific evidence but paying attention to and acting on the evidence, and the trend of the evidence at hand) and in its environmental health criteria recommendations. If the WHO EMF Program instead chooses to use the definitions of adverse impact and risk based on reacting to nothing short of conclusive scientific evidence, it fails to comply with the over-arching EU principle of health.

The World Health Organization has issued a draft framework to address the adequacy of scientific information, and accepted definitions of bioeffect, adverse health effect and hazard (WHO EMF Program Framework for Developing EMF Standards, Draft, October 2003). These definitions are not subject to the whim of organizations preparing public exposure standard recommendations. The WHO definition states that:

"(A)nnoyance or discomforts caused by EMF exposure may not be pathological per se, but, if substantiated, can affect the physical and mental well-being of a person and the resultant effect may be considered as an adverse health effect. A health effect is thus defined as a biological effect that is detrimental to health or well-being. According to the WHO Constitution, health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." **www.who.int/peh-emf**

The European Union Treaties Article 174

The EU policy (Article 174-2) requires that the precautionary principle be the basis for environmental protection for the public, and that protecting public health and taking preventative action before certainty of harm is proven is the foundation of the Precautionary Principle. It is directly counter to the principles used by ICNIRP and IEEE in developing their recommendations for exposure standards. Both bodies require proof of adverse effect and risk before amending the exposure standards; this Treaty requires action to protect the public when a reasonable suspicion of risk exists (precautionary action).

Article 174 (2) [ex Article 130r]

1. Community policy on the environment shall contribute to pursuit of the following objectives:
—preserving, protecting and improving the quality of the environment;
—protecting human health;
—prudent and rational utilisation of natural resources;
—promoting measures at international level to deal with regional or worldwide environmental problems.

2. Community policy on the environment shall aim at a high level of protection taking into account the diversity of situations in the various regions of the Community. It shall

be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source and that the polluter should pay. In this context, harmonization measures answering environmental protection requirements shall include, where appropriate, as a safeguard clause allowing Member States to take provisional measures, for non-economic environmental reasons, subject to a Community inspection procedure.

3. In preparing its policy on the environment, the Community shall take account of:

—available scientific and technical data;
—environmental conditions in the various regions of the Community;
—the potential benefits and costs of action or lack of action;
—the economic and social development of the Community as a whole and the balanced development of its regions.

http://www.law.harvard.edu/library/services/research/guides/international/eu/eu_legal_research_treaties.php

WHO ELF Environmental Health Criteria Monograph, June 2007

In 2007. the WHO EMF Program released its ELF Health Criteria Monograph and held a workshop in Geneva, Switzerland June 20-21st.

ELF Health Criteria Monograph

12.6 Conclusions

Acute biological effects have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection.

Consistent epidemiological evidence suggests that chronic low-intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. ***However, the evidence for a causal relationship is limited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted.*** (emphasis added).

The Monograph finds no reason to change the designation of EMF as a 2B (Possible) Human Carcinogen as defined by the International Agency for Cancer Research (IARC). In finding that ELF-EMF is classifiable as a possible carcinogen, it is inconsistent to conclude that no change in the exposure limits is warranted. If the Monograph confirms, as other review bodies have, that childhood leukemia occurs at least as low as the 3 mG to 4 mG exposure range, then ICNIRP limits of 1000 mG for 50 Hz and 60 Hz ELF exposures are clearly too high and pose a risk to the health of children.

The WHO Fact Sheet summarizes some of the Monograph findings but adds further recommendations.

"Potential long-term effects"

Much of the scientific research examining long-term risks from ELF magnetic field exposure has focused on childhood leukaemia. In 2002, IARC published a monograph classifying ELF magnetic fields as "possibly carcinogenic to humans. This classification was based on pooled analyses of epidemiological studies demonstrating a consistent pattern of a two-fold increase in childhood leukaemia associated with average exposure to residential power-frequency magnetic field above 0.3 to 0.4 μT. ***The Task Group concluded that additional studies since then do not alter the status of this classification."*** *(emphasis added)*

"International exposure guidelines"

"Health effects related to short-term, high-level exposure have been established and form the basis of two international exposure limit guidelines (ICNIRP, 1998; IEEE, 2002). At present, these bodies consider the scientific evidence related to possible health effects from long-term, low-level exposure to ELF fields insufficient to justify lowering these quantitative exposure limits."

"Regarding long-term effects, given the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia, the benefits of exposure reduction on health are unclear. In view of this situation, the following recommendations are given:

1) Government and industry should monitor science and promote research programmes to further reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure. Through the ELF risk assessment process, gaps in knowledge have been identified and these form the basis of a new research agenda.

2) Member States are encouraged to establish effective and open communication programmes with all stakeholders to enable informed decision-making. These may include improving coordination and consultation among industry, local government, and citizens in the planning process for ELF EMF-emitting facilities.

3) When constructing new facilities and designing new equipment, including appliances, low-cost ways of reducing exposures may be explored. Appropriate exposure reduction measures will vary from one country to another. However, policies based on the adoption of arbitrary low exposure limits are not warranted."

The last bullet in the WHO ELF Fact Sheet does not come from the Monograph, nor is it consistent with conclusions of the Monograph. The Monograph does call for prudent avoidance measures, one of which could reasonably be to establish numeric planning targets or interim limits for new and upgraded transmission lines and appliances used by children, for example. Countries should not be dissuaded by WHO staff, who unlike the authors of the Monograph, go too far in defining appropriate boundaries for countries that may wish to implement prudent avoidance in ways that best suit their population needs, expectations and resources. www.who.int/peh-emf/project/en

World Health Organization Report on Children's Health and Environment

Environmental Issue Report Number 29 from the World Health Organization (2002) cautions about the effects of radiofrequency radiation on children's health. As part of a publication on "Children's Health and Environment: A Review of Evidence" the World Health Organization (WHO) wrote:

> *"The possible adverse health effects in children associated with radiofrequency fields have not been fully investigated."*
>
> *"Because there are suggestions that RF exposure may be more hazardous for the fetus and child due to their greater susceptibility, prudent avoidance is one approach to keeping children's exposure as low as possible."*
>
> *"Further research is needed to clarify the potential risks of ELF-EMF and radiofrequency fields for children's health."*

International Agency for Research on Cancer (IARC)

A 2001 report by the WHO International Agency for Research on Cancer (IARC) concluded that ELF-EMF power frequency fields are a Category 2B (Possible) Human Carcinogen. These are power-frequency electromagnetic fields (50-Hz and 60-Hz electric power frequency fields).

The World Health Organization (WHO) is conducting the International Electromagnetic Fields (EMF) Project to assess health and environmental effects of exposure to static and time varying electric and magnetic fields in the frequency range of 1 – 300 gigahertz (GHz). Project goals include the development of international guidelines on exposure limits. This work will address radio and television broadcast towers, wireless communications transmission and telecommunications facilities, and associated devices such as mobile phones, medical and industrial equipment, and radars. It is a multi-year program that began in 1996 and will end in 2005. www.who.int/peh-emf

SCENIHR Opinion (European Commission Study of EMF and Human Health)

An independent Scientific Committee on newly emerging risks commissioned by the European Union released an update of its 2001 opinion on electromagnetic fields and human health in 2007. "The Committed addressed questions related to potential risks associated with interaction of risk factors, synergistic effects, cumulative effects, anti-microbial resistance, new technologies such as nanotechnologies, medical devices, tissue engineeringm blood products, fertility reduction, cancer of endocrine organs, physical hazards such as noise and electromagnetic fields and methodologies for assessing new risks." SCENIHR, 2007

SCENIHR Conclusions on Extremely low frequency fields (ELF fields)

The previous conclusion that ELF magnetic fields are possibly carcinogenic, chiefly based on childhood leukaemia results, is still valid. There is no generally accepted mechanism to explain how ELF magnetic field exposure may cause leukaemia.

For breast cancer and cardiovascular disease, recent research has indicated that an association is unlikely. For neurodegenerative diseases and brain tumours, the link to ELF fields remains uncertain. A relation between ELF fields and symptoms (sometimes referred to as electromagnetic hypersensitivity) has not been demonstrated.

SCENIHR Conclusions on Radiofrequency Radiation fields (RF fields)

Since the adoption of the 2001 opinion, extensive research has been conducted regarding possible health effects of exposure to low intensity RF fields. This research has investigated a variety of possible effects and has included epidemiologic, in vivo, and in vitro research. The overall epidemiologic evidence suggests that mobile phone use of less than 10 years does not pose any increased risk of brain tumour or acoustic neuroma. For longer use, data are sparse, since only some recent studies have reasonably large numbers of long-term users. Any conclusion therefore is uncertain and tentative. From the available data, however, it does appear that there is no increased risk for brain tumours in long-term users, with the exception of acoustic neuroma for which there is limited evidence of a weak association. Results of the so-called Interphone study will provide more insight, but it cannot be ruled out that some questions will remain open.

SCENIHR Conclusions on Sensitivity of Children

Concerns about the potential vulnerability of children to RF fields have been raised because of the potentially greater susceptibility of their developing nervous system; in addition, their brain tissue is more conductive than that of adults since it has a higher water content and ion concentration, RF penetration is greater relative to head size, and they have a greater absorption of RF energy in the tissues of the head at mobile telephone frequencies. Finally, they will have a longer lifetime exposure.

Few relevant epidemiological or laboratory studies have addressed the possible effects of RF field exposure on children. Owing to widespread use of mobile phones among children and adolescents and relatively high exposures to the brain, investigation of the potential effect of RF fields in the development of childhood brain tumour is warranted. The characteristics of mobile phone use among children, their potential biological vulnerability and longer lifetime exposure make extrapolation from adult studies problematic.

There is an ongoing debate on possible differences in RF absorption between children and adults during mobile phone usage, e.g. due to differences in anatomy (Wiart et al. 2005, Christ and Kuster, 2005). Several scientific questions like possible differences of the dielectric tissue parameters remain open. The anatomical development of the nervous system is finished around 2 years of age, when children do not yet use mobile phones although baby phones have recently been introduced. Functional development, however, continues up to adult age and could be disturbed by RF fields.

Health Protection Agency (Formerly the NRPB - United Kingdom)

The National Radiation Protection Board or NRPB (2004) concluded, based on a review of the scientific evidence, that the most coherent and plausible basis from which guidance could be developed on exposures to ELF concerned weak electric field interactions in the brain and CNS (NRPB, 2004). A cautious approach was used to indicate thresholds for possible adverse health effects.

> *"Health Effects - It was concluded from the review of scientific evidence (NRPB, 2004b) that the most coherent and plausible basis from which guidance could be developed on exposures to ELF EMFs concerned weak electric field interactions in the brain and CNS (NRPB, 2004). A cautious approach was used to indicate thresholds for possible adverse health effects."*
>
> *"The brain and nervous system operate using highly complex patterns of \electrical signals. Therefore, the basic restrictions are designed to limit the electric fields and current densities in these tissues so as to not adversely affect their normal functioning. The adverse effects that might occur cannot easily be characterized according to presenting signs or symptoms of disease or injury. They represent potential changes to mental processes such as attention and memory, as well as to regulatory functions with in the body. Thus, the basic restrictions should not be regarded as precisely determined values below which no adverse health effects can occur and above which clearly discernible effects will happen. The do, however, indicate an increasing likelihood of effects occurring as exposure increases above the basic restriction values."*
>
> *"From the results of the epidemiological investigations, there remain concerns about a possible increased risk of child leukaemia associated with exposure to magnetic fields above about 0.4 uT (*4 mG*). In this regard, it is important to consider the possible need for further precautionary measures."*

This recent statement by the UK Health Protection Agency clearly indicates that the current guidelines may not be protective of public health. Yet, the reference levels used in the United Kingdom remain at 5000 mG for 50 Hz power frequency fields for occupational exposure and 1000 mG for public exposure.

US Government Radiofrequency Interagency Working Group Guidelines Statement

The United States Radiofrequency Interagency Working Group (RFIAWG) cited concerns about current federal standards for public exposure to radiofrequency radiation in 1999 (Lotz, 1999 for the Radiofrequency Interagency Working Group)

> *"Studies continue to be published describing biological responses to nonthermal ELF-modulated RF radiation exposures that are not produced by CW (unmodulated) radiation. These studies have resulted in concern that 'exposure guidelines based on thermal effects, and using information and concepts (time-averaged dosimetry, uncertainty factors) that mask any differences between intensity-modulated RF radiation exposure and CW exposure, do not directly address public exposures, and therefore may not adequately protect the public."*

The United States government Federal Radiofrequency Interagency Working Group has reviewed the existing ANSI/IEEE RF thermal-based exposure standard upon which the FCC limit is based. This Working Group was made up of representatives from the US government's National Institute for Occupational Safety and Health (NIOSH), the Federal Communications Commission (FCC), Occupational Health and Safety Administration (OSHA), the Environmental Protection Agency (US EPA), the National Telecommunication and Information Administration, and the US Food and Drug Administration (FDA).

On June 17, 1999, the RFIAWG issued a Guidelines Statement that concluded the present RF standard "may not adequately protect the public". The RFIAWG identified fourteen (14) issues that they believe are needed in the planned revisions of ANSI/IEEE RF exposure guidelines including "to provide a strong and credible rationale to support RF exposure guidelines". In particular, the RFIAWG criticized the existing standards as not taking into account chronic, as opposed to acute exposures, modulated or pulsed radiation (digital or pulsed RF is proposed at this site), time-averaged measurements that may erase the unique characteristics of an intensity-modulated RF radiation that may be responsible for reported biologic effects, and stated the need for a comprehensive review of long-term, low-level exposure studies, neurological-behavioral effects and micronucleus assay studies (showing genetic damage from low-level RF).

The existing federal standards may not be protective of public health in critical areas. The areas of improvement where changes are needed include: a) selection of an adverse effect level for chronic exposures not based on tissue heating and considering modulation effects; b) recognition of different safety criteria for acute and chronic exposures at non-thermal or low-intensity levels; c) recognition of deficiencies in using time-averaged measurements of RF that does not differentiate between intensity-modulated RF and continuous wave (CW) exposure, and *therefore may not adequately protect the public.*

As of 2007, requests to the RFIAWG on whether these issues have been satisfactorily resolved in the new 2006 IEEE recommendations for RF public safety limits have gone unanswered (BioInitiative Working Group, 2007).

United Kingdom - Parliament Independent Expert Group Report (Stewart Report)

The Parliament of the United Kingdom commissioned a scientific study group to evaluate the evidence for RF health and public safety concerns. In May of 2000, the United Kingdom Independent Expert Group on Mobile Phones issued a report underscoring concern that standards are not protective of public health related to both mobile phone use and exposure to wireless communication antennas.

Conclusions and recommendations from the Stewart Report (for Sir William Stewart) indicated that the Group has some reservation about continued wireless technology expansion without more consideration of planning, zoning and potential public health concerns. Further, the Report acknowledges significant public concern over community siting of mobile phone and other communication antennas in residential areas and near schools and hospitals.

> *"Children may be more vulnerable because of their developing nervous system, the greater absorption of energy in the tissue of the head and a longer lifetime of exposure."*
>
> *"The siting of base stations in residential areas can cause considerable concern and distress. These include schools, residential areas and hospitals."*
>
> *" There may be indirect health risks from living near base stations with a need for mobile phone operators to consult the public when installing base stations."*
>
> *"Monitoring should be expecially strict near schools, and that emissions of greatest intensity should not fall within school grounds."*
>
> *"The report recommends "a register of occupationally exposed workers be established and that cancer risks and mortality should be examined to determine whether there are any harmful effects."* (IEGMP, 2000)

Food and Drug Administration (US FDA)

The Food and Drug Administration announced on March 28, 2007 it is contracting with the National Academy of Science to conduct a symposium and issue a report on additional research needs related to possible health effects associated with exposure to radio frequency energy similar to those emitted by wireless communication devices. The National Academy of Sciences will organize an open meeting of national and international experts to discuss the research conducted to date, knowledge gaps, and additional research needed to fill those gaps. The workshop will consider the scientific literature and ongoing research from an international perspective in order to avoid duplication, and in recognition of the international nature of the scientific community and of the wireless industry.

Funding for the project will come from a Cooperative Research and Development Agreement (CRADA) between the Food and Drug Administration's Center for Devices and Radiological Health and the Cellular Telecommunications and Internet Association (CTIA). http://www.fda.gov/cellphones/index.html

National Institutes for Health - National Toxicology Program

The National Toxicology Program (NTP) is a part of the National Institute for Environmental Health Sciences, National Institutes for Health. Public and agency comment has been solicited on whether to add radiofrequency radiation to its list of substances to be tested by NTP as carcinogens. In February 2000 the FDA made a recommendation to the NPT urging that RF be tested for carcinogenicity (www.fda.gov.us). The recommendation is based in part on written testimony stating:

> *" Animal experiments are crucial because meaningful data will not be available from epidemiological studies for many years due to the long latency period between exposure to a carcinogen and the diagnosis of a tumor.*
>
> *"There is currently insufficient scientific basis for concluding either that wireless communication technologies are safe or that they pose a risk to millions of users."*
>
> *"FCC radiofrequency radiation guidelines are based on protection from acute injury from thermal effects of RF exposure* and may not be protective *against any non-thermal effects of chronic exposures."*

In March of 2003, the National Toxicology Program issued a Fact Sheet regarding its toxicology and carcinogenicity testing of radiofrequency/microwave radiation. These studies will evaluate radiofrequency radiation in the cellular frequencies.

> *"The existing exposure guidelines are based on protection from acute injury from thermal effects of RF exposure. Current data are insufficient to draw definitive conclusions concerning the adequacy of these guidelines to be protective against any non-thermal effects of chronic exposures. "*

US Food and Drug Administration

In February of 2000, Russell D. Owen, Chief of the Radiation Biology Branch of the Center for Devices and Radiological Health, US Food and Drug Administration (FDA) commented that there is:

> *"currently insufficient scientific basis for concluding whether wireless communication technologies pose any health risk."*
>
> *"Little is known about the possible health effects of repeated or long-term exposures to low level RF of the sort emitted by such devices."*

"Some animal studies suggest the possibility for such low-level exposures to increase the risk of cancer..."

Dr. Owen's comments are directed to users of cell phones, but the same questions are pertinent for long-term RF exposure to radiofrequency radiation for the larger broadcast transmissions of television, radio and wireless communications (Epidemiology Vol. 1, No. 2 March 2000 Commentary). The Food and Drug Administration signed an agreement (CRADA agreement) to provide funding for immediate research into RF health effects, to be funded by the Cellular Telephone Industry of America. The FDA no longer assures the safety of users. No completion date has been set.

National Academy of Sciences - National Research Council

An Assessment of Non-Lethal Weapons Science and Technology by the Naval Studies Board, Division of Engineering and Physical Sciences (National Academies Press (2002) has produced a report that confirms the existence of non-thermal bioeffects from information transmitted by radiofrequency radiation at low intensities that cannot act by tissue heating (prepublication copy, page 2-13).

In this report, the section on Directed-Energy Non-Lethal Weapons it states that:

"The first radiofrequency non-lethal weapons, VMADS, is based on a biophysical susceptibility known empirically for decades. More in-depth health effects studies were launched only after the decision was made to develop that capability as a weapon. The heating action of RF signals is well understood and can be the basis for several additional directed-energy weapons. <u>Leap-ahead non-lethal weapons technologies will probably be based on more subtle human/RF interactions in which the signal information within the RF exposure causes an effect other than simply heating: for example, stun, seizure, startle and decreased spontaneous activity.</u> Recent developments in the technology are leading to ultrawideband, very high peak power and ultrashort signal capabilities, suggesting the the phase space to be explored for subtle, uyet potentially effective non-thermal biophysical susceptibilities is vast. Advances will require a dedicated effort to identify useful susceptibilities."

Page 2-13 of the prepublication report (emphasis added)

This admission by the Naval Studies Board confirms several critical issues with respect to non-thermal or low-intensity RF exposures. First, it confirms the existence of bioeffects from non-thermal exposure levels of RF. Second, it identifies that some of these non-thermal effects can be weaponized with bioeffects that are incontrovertibly adverse to health (stun, seizure, startle, decreased spontaneous activity). Third, it confirms that there has been knowledge for decades about the susceptibility of human beings to non-thermal levels of RF exposure. Fourth, it provides confirmation of the concept that radiofrequency interacts with humans based on the RF information content (signal information) rather than heating, so it can occur at subtle energy levels, not at high levels associated with tissue heating. Finally, the report indicates that a dedicated scientific research effort is needed to really understand and refine non-thermal RF as a weapon, but it is promising enough for continued federal funding.

The IEEE (United States)

IEEE ICES SCC-28 SC-4 Subcommittee (Radiofrequency/Microwave Radiation)
Members of the ICES SCC-28 SC-4 committee presented their views and justifications in a Supplement to the Bioelectromagnetics Journal (2003). It offers a window into the thinking that continues to support thermal-only risks, and on which the current United States IEEE recommendations have been made. The United States Federal Communications Commission (FCC) has historically based its federally-mandated public and occupational exposure standards on the recommendations of the IEEE.

Radiofrequency/Microwave Radiation
IEEE's original biological benchmark for setting human exposure standards (on which most contemporary human standards are based) is disruption of food-motivated learned behavior in subject animals. For RF, it was based on short, high intensity RF exposures that were sufficient to result in changes in animal behavior.

"The biological endpoint on which most contemporary standards are based is disruption of food-motivated learned behavior in subject animals. The threshold SAR for behavioral disruption has been found to reliably occur between 3 and 9 W/kg across a number of animal species and frequencies; a whole-body average SAR of 4 W/kg is considered the threshold below which adverse effects would not be expected. To ensure a margin of safety, the threshold SAR is reduced by a safety factor of 10 and 50 to yield basic restrictions of 0.4 W/kg and 0.08 W/kg for exposures in controlled (occupational) and uncontrolled (public) environments, respectively." (Osepchuk and Petersen, 2003).

The development of public exposure standards for RF is thus based on acute, but not chronic exposures, fails to take into account intermittent exposures, fails to consider special impacts of pulsed RF and ELF-modulated RF, and fails to take into account bioeffects from long-term, low-intensity exposures that may lead to adverse health impacts over time.

BEMS Supplement 6 (Journal of the Bioelectromagnetics Society)

BEMS Supplement 6 was prepared in support of the IEEE SC-4 committee RF recommendations. In explaining and defending revised recommendations on RF limits contained within C.95.1, some key members took out space in Bioelectromagnetics (the Journal of the Bioelectromagnetic Society) to present papers ostensibly justifying a relaxation of the existing IEEE RF standards, rather than making the standards more conservative to reflect the emerging scientific evidence for both bioeffects and adverse health impacts.

Several clues are contained in the BEMS Supplement 6 to understand how the SC-4 IEEE C.95 revision working group and the ICES could arrive at a decision to not to recommend tighter limits on RF exposure. Not one but two definitions of "adverse effect" are described, one by Osepchuk/Petersen (2003) and another by the working group itself (D'Andrea et al, 2003). Both set a very high bar for demonstration of proof, and both are ignored in the final recommendations by the SC-4 Subcommittee.

Second, many of the findings presented in the papers by individual authors in the BEMS Supplement 6 do report that RF exposures are linked to bioeffects and to adverse effects; but these findings are evidently ignored or dismissed by the SC-4 Subcommittee, ICES and by the eventual adoption of these recommendations by the full IEEE membership (in 2006). Even with a very high bar of evidence set by the SC-4 Subcommittee (and two somewhat conflicting definitions of adverse effect against which all scientific papers were reviewed and analyzed); there is clear sign that the "deal was done' regardless of even some of the key Subcommittee member findings reporting such effects at exposure levels below the existing limits.* sidebar

The SC-4 Subcommittee has developed a new and highly limited definition on RF effects, adverse effects and hazards that is counter to the WHO Constitution Principle on Health. The definition as presented by D'Andrea et al (2003, page S138) is based on the SC-4 IEEE C.95 revision working group definition of adverse effect:

"An adverse effect is a biological effect characterized by a harmful change in health. For example, such changes can include organic disease, impaired mental function, behavioral disfunction, reduced longevity, and defective or deficient reproduction. Adverse effects do not include: biological effects without detrimental health effect, changes in subjective feelings of well-being that are a result of anxiety about RF effects or impacts of RF infrastructure that are not related to RF emissions, or indirect effects caused by electromagnetic interference with electronic devices. An adverse effects exposure level is the condition or set of conditions under which an electric, magnetic or electromagnetic field has an adverse effect."

Further, the working group extended its definition to include that of Michaelson and Lin (1987) which states:

"If an effect is of such an intense nature that it compromises the individual's ability to function properly or overcomes the recovery capability of the individual, then the 'effect' may be considered a hazard. In any discussion of the potential for 'biological effects' from exposure to electromagnetic energies we must first determine whether any 'effect' can be shown; and then determine whether such an observed 'effect' is hazardous."

The definition of adverse effect according to Osepchuk and Petersen (2003) reported in the same BEMS Supplement 6 is:

"An adverse biological response is considered any biochemical change, functional impairment, or pathological lesion that could impair performance and reduce the ability of an organism to respond to additional challenge. Adverse biological responses should be distinguished from biological responses in general, which could be adaptive or compensatory, harmful, or beneficial. "

In contrast, the World Health Organization draft framework has accepted definitions of bioeffect, adverse health effect and hazard (WHO EMF Program Framework for Developing EMF Standards, Draft, October 2003). These definitions are not subject to the whim of organizations preparing public exposure standard recommendations. The WHO definition states that:

"(A)nnoyance or discomforts caused by EMF exposure may not be pathological per se, but, if substantiated, can affect the physical and mental well-being of a person and the resultant effect may be considered as an adverse health effect. A health effect is thus defined as a biological effect that is detrimental to health or well-being. According to the WHO Constitution, health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity."

The SC-4 definitions require proof that RF has caused organic disease or other cited effects that qualify. The burden of proof is ultimately shifted to the public, that bears the burden of unacknowledged health effects and diseases, where the only remedy is proof of illness over a large population of affected individuals, over a significant amount of time, and finally, delays until revisions of the standards can be implemented. The results of studies and reviews in the BEMS Supplement 6 already acknowledge the existence of bioeffects and adverse effects that occur at non-thermal exposure levels (below current FCC and ICNIRP standards that are supposedly protective of public health. However, they go on to ignore their own findings, and posit in advance that adverse effects seen today will, even with chronic exposure, not conclusively reveal disease or dysfunction tomorrow at exposure levels below the existing standards.

Sidebar: Quotes from BEMS Supplement 6

a) Studies and reviews where bioeffects likely to lead to adverse health effects with chronic exposure are reported;
b) adverse effects which are already documented;
c) studies where non-thermal RF effects are reported and unexplained;
d) effects are occurring below current exposure limits, and
e) conclusions by authors they cannot draw conclusions about hazards to human health

These quotes appear in articles presented by the IEEE SC-4 Subcommittee in BEMS Supplement 6. Despite these acknowledged gaps in information, lack of consistency in studies, abundant conflicting evidence documenting low level RF effects that can resulting serious adverse health impacts (DNA damage, cognitive impairment, neurological deficits, cancer, etc), and other clear instances of denial of ability to predict human health outcomes, the IEEE SC-4 Subcommittee has proposed recommendations to relax the existing limits.

D'Andrea et al., 2003a (Behavioral and Cognitive Effects of Microwave Exposure S39-S62)

"Reports of change of cognitive function (memory and learning) in humans and laboratory animals are in the scientific literature. Mostly, these are thermally mediated effects, but other low level effects are not so easily explained by thermal mechanisms." S39 Abstract

Elwood in Epidemiological Studies of Radiofrequency Exposures and Human Cancer (S63-S73)

"Studies are unable to confidently exclude any possibility of increased risk of cancer." S63 Abstract.

"Further research to clarify the situation is justified. Priorities include further studies of leukemia in both adults and children, and of cranial tumors in relationship to mobile phone use." S63 Abstract

"Although the epidemiological evidence in total suggests no increased risk of cancer, the results cannot be unequivocally interpreted in terms of cause and effect." S63 Abstract

D'Andrea et al., 2003b (Microwave Effects on the Nervous System S107-S147

"Low-level exposures that report alterations of the (blood-brain barrier) BBB remain controversial." S10 Abstract

"Research with isolated brain tissue has provided new results that do not seem to rely on thermal mechanisms." S107 Abstract

"Studies of individuals who are reported to be sensitive to electric and magnetic fields are discussed." S107 Abstract

"In this review of the literature, it is difficult to draw any conclusions concerning hazards to human health." S107 Abstract

"At lower levels of exposure biological effects may still occur but thermal mechanisms are not ruled out." S107 Abstract

"Based on a review of the literature presented here, it is difficult to draw conclusions concerning hazards to human health." " At lower levels of exposure, biological effects may still occur but thermal mechanisms are not ruled out." " There are too few studies to draw conclusions about the health effects of the low level findings" (on morphological effects of RF on animals).

"Other studies report low level effects where thermal mechanisms cannot explain the results." (effects of MW on neurochemistry).

"Additional work is needed to further evaluate the effects of RF exposure on working memory and cognition." (S138-S139)

Conclusions:

"Some reports of biological effects that cannot be explained by thermal mechanisms are in the scientific literature. These will require much more research to fully understand the mechanisms involved. Regardless of the mechanism, reports of effects that are at or below current recommended safety guidelines deserve rapid evaluation." (S140)

Proceedings of the NATO Advanced Research Workshop – Mechanisms of the Biological Effect on Extra High Power Pulses (EHPP) and UNESCO/WHO/IUPAB Seminar "Molecular and Cellular Mechanisms of Biological Effects of EMF" held March 2005, Yerevan, Armenia.

The proceedings conclude that "*the authors agreed with one main conclusion from these meeting(s): that in the future worldwide harmonization of standards have to be based on biological responses, rather than computed values*". The authors included 47 scientists, engineers, physicians and policy makers from 21 countries from Europe, North and South America, and Asia.

> *"The ICNIRP Guidelines for radiofrequency electromagnetic exposure are based only on thermal effects, and completely neglects the possibility of non-thermal effect."*
>
> *"The guidelines of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) specify the quantative characteristics of EMF used to specify the basic restrictions are current density, specific absorption rate (SAR) and power density, i.e., the energetic characteristics of EMF. However, experimental data on energy-dependency of biological effects by EMF have shown that the SAR approach, very often, neither adequately describes or explains the real value of EMF-induced biological effects on cells and organisms, for at least two reasons: a) the non-linear character of EMF-induced bioeffects due to the existence of amplitude, frequency and 'exposure time-windows' and b) EMF-induced bioeffects significantly depend on physical and chemical composition of the surrounding medium."* (Preface pages XI – XIII).

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SECTION 5

EVIDENCE FOR EFFECTS ON GENE AND PROTEIN EXPRESSION

(Transcriptomic and Proteomic Research)

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I. INTRODUCTION

Daily exposure to electromagnetic fields (EMF), including extremely low frequency magnetic fields (ELF MF) and radiofrequency (RF) EMF, in the environment has raised public concerns about whether they have harmful consequences on human health. Several epidemiological studies suggest that exposure to EMF might associate with an elevated risk of cancer and other diseases in humans (reviewed in [Feychting et al., 2005]). To explain and/or support epidemiological observations, many laboratory studies have been conducted, but the results were controversial and no clear conclusion could be drawn to assess EMF health risk.

It is reasoned that one of the priorities in EMF research is to elucidate the biological effects of EMF exposure and the underlining mechanisms of action. Gene and protein are key players in organisms, and it has been assumed that any biological impact of EMF must be mediated by alterations in gene and protein expression [Phillips et al., 1992; Wei et al., 1990]. For example, heat shock protein, c-myc, and c-jun have been identified as EMF responsive genes and/or proteins in certain biological systems. In order to reveal the global effects of EMF on gene and protein expression, transcriptomics and proteomics, as high-throughput screening techniques (HTSTs), were eventually employed in EMF research with an intention to screen potential EMF-responsive genes and/or proteins without any bias. In 2005, WHO organized a Workshop on Application of Proteomics and Transcriptomics in EMF Research in Helsinki, Finland to discuss the related problems and solutions in this field [Leszczynski 2006; Leszczynski and Meltz 2006]. Later the journal Proteomics published a special issue devoted to the application of proteomics and transcriptomics to EMF research. This review aims to summarize the current research progress and discuss the applicability of HTSTs in the field.

II. ELF MF

II A. TRANSCRIPTOMICS

Binninger and Ungvichian firstly measured purified mRNA levels of total RNA from MF- and sham-exposed yeast cells and reported that the levels of a significant proportion of mRNAs were altered in response to continuous exposure to 20 T 60 Hz MF over a period of approximately 15 cell generations (24 h) [Binninger and Ungvichian 1997]. Unfortunately, no reproducible genes (polypetides) were identified in this study although the authors consistently found different proportions of transcripts whose abundances were altered in all four replication experiments.

Wu *et al.* have applied differential display reverse transcriptase–polymerase chain reaction (DD-RT-PCR) and Northern blotting to screen MF-responsive gene in Daudi cells. The cells were exposed to 0.8 mT of 50 Hz MF for 24 h. The authors screened out two candidate genes in Daudi cells and one was identified as a MF-responsive gene *ceramide glucosyltransferase*. They further found time-dependent changes in the transcription of *ceramide glucosyltransferase* induced by 0.8 mT MF [Wu et al., 2000]. With the help of DD-RT-PCR, Olivares-Banuelos *et al* reported that exposure to 0.7 mT 60 Hz MF for 7 days, 4 h a day (2 h in the morning and 2 h in the afternoon), changed the global transcription profile of chromaffin cells. Eight RT-PCR products which correspond to six genes were identified, including *phosphoglucomutase*-1, *neurofibromatosis-2 interacting protein*, *microtubule associated protein*-2, *thiamine pyrophosphokinase*, and two hypothetical proteins (RNOR02022103 and ROR01044577). In addition, the authors found that presumed regulatory regions of these genes contained CTCT-clusters [Olivares-Banuelos et al., 2004], which has been identified as an electromagnetic field-responsive DNA element regulating gene expression [Goodman and Blank 2002].

Balcer-Kubiczek *et al.* have applied the two-gel cDNA library screening method (BIGEL) to screen MF-responsive genes, in which the gel arrays contained a total of

960 cDNAs selected at random from the cDNA library. The HL 60 cells were exposed to 2 mT of 60 Hz square wave MF for 24 h. Four candidate genes were shown responsive to the MF exposure, but could not be confirmed by following Northern analysis. Furthermore, the authors found that these four candidates and another four selected genes (*MYC*, *HSP70*, *RAN* and *SOD1*) did not react to either square wave or sine wave 60 Hz MF at 2 mT for 24 h [Balcer-Kubiczek et al., 2000]. However, the cellular responses to square wave and sine wave 60 Hz MF might be different. In order to systematically evaluate the effect of 60 Hz MF on gene expression in HL 60 cells, it is necessary for the authors to screen 60 Hz sine wave MF responsive candidate genes in HL 60 cells with BIGEL method as well, and then, perform validation with Northern blotting for these candidates.

Using cDNA arrays containing 588 cancer-related genes, Loberg *et al.* analyzed gene expression in normal (HME) and transformed (HBL-100) human mammary epithelial cells and human promyelocytic leukemia (HL60) cells after exposure to 60 Hz MF at intensity of 0.01 or 1.0 mT for 24 h. The authors reported that several genes were identified in MF-exposed cells whose expressions were increased by at least two folds or decreased by 50% or more, but no gene was found to be differentially expressed in each of three independent exposures for any cell type, and no relationship between exposure intensity and differential gene expression was found [Loberg et al., 2000].

In order to obtain a more global evaluation, genome-wide microarray screening methods were applied to identify genes responding to ELF MF in certain types of cells. By application of cDNA microarray, Nakasono *et al.* have investigated the effect of 50 Hz MF below 300 mT on gene expression in yeast. The authors reported that several genes were found differentially expressed in yeast cells with medium to low confidence level (CL) after exposure to 10, 150 and 300 mT for 24 h. Among these genes, seven showed a dose-response relationship in the normalized ratio data and three genes showed a reproducible change for all three intensities. They also proposed that these genes should be re-examined by methods with greater sensitivity or by quantitative methods, such as real-time PCR. On the other hand, no high-confidence expression changes were observed for genes that are involved in heat-shock response, DNA repair, respiration, protein synthesis, or cell cycle. Thus, they concluded that 50 Hz MF up to 300 mT did not appear to affect gene expression linked to either defined cell processes stated above or unknown cell responses in investigated model eukaryotic cells [Nakasono et al., 2003]. Unfortunately, only single experiment for array analysis was performed in this study.

Recently, a similar study was conducted by Luceri *et al.* to investigate the global gene response to 50 Hz MF in human lymphocytes and yeast cells. These two types of cells were exposed to MF at intensity of 100 T, 10 T and 1 T for 18 h. As a result, in lymphocytes, one gene was found down-regulated at 100 T, one down-regulated gene and two up-regulated genes were screened out at 10 T, and no gene was detected changed at 1 T. As to the yeast cells, the results showed 2, 15 and 2 genes as differentially expressed (mainly down-regulated) after exposure to 100, 10 and 1 T, respectively, in which SPS100 gene was consistently up-regulated after exposure to 50 Hz MF at all three intensities. But no genes were found differentially expressed when the authors analyzed the data by other statistical methods. Thus, the authors concluded that 50 Hz MF did not affect gene expression in these two types of cells and the variations of a few genes mentioned above could be due to experimental noise [Luceri et al., 2005]. However, it is necessary to examine the candidates, especially the SPS100 gene, to validate whether they were real "un-responsive" genes.

In Henderson's report, human umbilical vein endothelial cells (HUVEC) were exposed to various patterns and intensities of 50 Hz MF, including continuous exposure at a two intensities (10 and 700 T), intermittent exposure (60 min on/ 30 min off) at a single intensity (700 T), and continuous exposure to a variable-intensity fields (10-30 T). The transcriptional response of the cells was investigated using oligonucleotide microarrays containing up to 30, 000 unique features. Although different genes were identified where their expressions appeared to be affected by exposure to MF in individual experiments, none of these genes were regulated in the same manner in subsequent repetition experiments [Henderson et al., 2006].

Antonini *et al* reported that intermittent exposure (5 min on/5 min off) to 50 Hz MF at flux densities of 2 mT for 16 h could change gene expression in human neuroblastoma cell line SH-SY5Y by application of whole-genome Human Unigene RZPD-2 cDNA array which contains about 75, 000 cDNA clones. Several genes were found down- or up-regulated at least five-fold after ELF MF exposure and the authors concluded that SH-SY5Y cells were sensitive to ELF MF [Antonini et al., 2006]. However, no reports indicated that these differentially expressed genes were confirmed by other methods.

Lupke *et al* investigated the effect of ELF MF on gene expression profiling in human umbilical cord blood-derived monocytes using the same Unigene RZPD-2. The results indicated that 0.1 mT 50 Hz MF exposure for 45 minutes altered the expressions of 986 genes involved in metabolism, cellular physiological processes, signal transduction, and immune response, among them, five genes were significantly regulated. Furthermore, the authors analyzed several genes by real-time RT-PCR and one ELF MF candidate responsive gene IL15RA was confirmed. However, this study only did single array analysis for pooling sample from 78 donors and two independent real-time RT-PCR analyses for samples from 5 and 6 different donors. The authors did not report the examinations of other candidates with real-time RT-PCR analysis [Lupke et al., 2006].

II B. PROTEOMICS

Nakasono *et al.* has investigated the effects of protein expression in model system such as *Escherichia coli* and *Saccharomyces cerevisiae* using two dimensional gels electrophoresis (2-DE) method. When the bacterial cells were exposed to each MF at 5-100 Hz under aerobic conditions (6.5 h) or at 50 Hz under anaerobic conditions (16 h) at the maximum intensity (7.8 to 14 mT), no reproducible changes were observed in the 2D gels. However, the stress-sensitive proteins did respond to most stress factors, including temperature change, chemical compounds, heavy metals, and nutrients. The authors concluded that the high-intensity ELF MF (14 mT at power frequency) did not act as a general stress factor [Nakasono and Saiki 2000]. When using *Saccharomyces cerevisiae* as a model system, Nakasono *et al.* reported that no reproducible changes in the 2D gels were observed in yeast cells after exposure to 50 Hz MF at the intensity up to 300 mT for 24 h [Nakasono et al., 2003]. In this study, only three sets of gels from three independent experiments were analyzed.

Li *et al.* have performed a proteomics approach to investigate the changes of protein expression profile induced by ELF MF in human breast cancer cell line MCF-7. With help of 2-DE and data analysis on nine gels for each group, 44 differentially expressed protein spots were screened in MCF-7 cells after exposure to 0.4 mT 50 Hz MF for 24 h. Three proteins were identified by LC-IT Tandem MS as RNA binding protein regulatory subunit, proteasome subunit beta type 7 precursor, and translationally controlled tumor protein, respectively [Li et al 2005]. Further investigations, such as Western blotting, are required to confirm these ELF responsive candidate proteins.

Using 2-D Fluorescence Difference Gel Electrophoresis (2-D DIGE) technology and MS in a blind study, Sinclair *et al* have investigated the effects of ELF MF on the proteomes of wild type *Schizosaccharomyces pombe* and a Sty1p deletion mutant which displays increased sensitivity to a variety of cellular stresses. The yeast cells were exposed to 50 Hz EMF at field strength of 1 mT for 60 min. While this study identified a number of protein isoforms that displayed significant differential expressions across experimental conditions, there was no correlation between their patterns of expression and the ELF MF exposure regimen. The authors concluded that there were no significant effects of ELF MF on the yeast proteome at the sensitivity afforded by 2D-DIGE. They hypothesized that the proteins identified in the experiments must be sensitive to subtle changes in culture and/or handling conditions. Based on their experience, they suggested to the community that the interpretation of proteomic data in a biological context should be treated with caution [Sinclair et al., 2006].

II C. SUMMARY

Generally, recent studies on global gene and protein expression responding to ELF MF have been conducted in different biological systems by applications of HTSTs. Only a few studies reported to identify ELF MF responsive genes successfully. For example Wu *et al.* identified *ceramide glucosyltransferase* as a MF-responsive gene in Daudi cells [Wu et al., 2000] and Olivares-Banuelos *et al.* identified six ELF MF genes in chromaffin cells [Olivares-Banuelos et al., 2004] with the help of DD-RT-PCR and Northern blotting analysis; by combining cDNA array analysis with real-time RT-PCR confimation, Lupke *et al.* identified IL15RA as ELF MF responsive genes in human monocytes [Lupke et al., 2006]. Although many transcriptome and proteome analysis showed that ELF MF exposure could change gene and/or protein expression in certain cell types [Antonini et al., 2006; Binninger and Ungvichian 1997; Li et al., 2005], there are lack of confirmation to determine if they are real ELF MF responsive genes or proteins. Therefore, it is a priority to conduct confirmation experiments to demonstrate the author's findings.

As to those negative reports, few or no genes and proteins were found significantly changed according to their statistical analysis and screening standards. But these few genes and proteins were neither reproducible [Henderson et al., 2006; Nakasono et al., 2003; Sinclair et al., 2006]nor confirmed by other methods [Balcer-Kubiczek et al., 2000], and the changes were not related to ELF MF exposure [Loberg et al., 2000; Luceri et al., 2005; Nakasono et al., 2003]. Therefore, these studies are also needed to be replicated or verified.

III. RF EMF

III A. TRANSCRIPTOMICS

In an initial study utilizing membrane-based cDNA microarray, Harvey and French studied the effects of 864.3 MHz (CW) on HMC-1 human monocytes. The exposure was carefully controlled and averaged at an SAR of 7 W/kg, almost double the exposure level of established adverse effects. Three 20 min exposures were performed at 4-h intervals daily for 7 days. cDNA microarray analyses revealed consistent alterations in steady-state mRNA levels of 3 of the 558 genes represented on the membranes including one proto-oncogene *c-kit* (increased), one apoptosis-associated gene *DAD-1* (decreased) and one potential tumor suppressor gene *NDPK* (decreased) [Harvey and French 1999]. However, there were considerable variabilities between the two experiments reported and the fold change of each differentially expressed gene was small (< 1.5 folds). Meanwhile, the authors did not use other methods to confirm the results.

Pacini *et al.* investigated the effect of gene expression in human skin fibroblasts by using cDNA arrays including 82 genes, and reported that exposure to GSM 902.4 MHz RF EMF at an average SAR of 0.6 W/kg for 1 h increased the expression of 14 genes which function in mitogenic signal transduction, cell growth and apoptosis controlling. The authors further demonstrated a significant increase in DNA synthesis and intracellular mitogenic second messenger formation which were matched the high expression of MAP kinase family genes [Pacini et al., 2002]. The authors suggested that the RF EMF exposure has significant biological effects on human skin fibroblasts.

However, only one experiment was performed in array analysis and no more experiment was made by the authors to confirm the array analysis result.

With help of cDNA microarray, Leszczynski *et al.* reported that exposure to GSM 900 MHz RF EMF at an average SAR of 2.4 W/kg for 1 h changed expression of 3600 genes, including down-regulated genes involved in forming the Fas/TNFa apoptotic pathway in human endothelial cell line EA.hy926 [Leszczynski et al., 2004]. The authors performed three separate experiments in array analysis, but no confirmation experiments were conducted to validate the array analysis result. Recently, Leszczynski group compared the global gene response of two human endothelial cells, EA.hy926 and its variant EA.hy926v1 to RF EMF and reported that the same genes were differently affected by the exposure to GSM 900 MHz RF EMF at an average SAR of 2.8 W/kg for 1 h in each of the cell lines [Nylund and Leszczynski 2006]. Similarly, no reports indicated that the differentially expressed genes in this study were confirmed by other methods.

Lee *et al.* used the serial analysis of gene expression (SAGE) method to measure the RF EMF effect on genome scale gene expression in HL 60 cells. The cells were exposed to 2.45 GHz RF EMF at an average SAR of 10 W/kg for 2 h and 6 h. The authors observed that 221 genes and 759 genes altered their expression after 2 h exposure and 6 h exposure respectively. Functional classification of the affected genes revealed that apoptosis-related genes were among the up-regulated ones and the cell cycle genes among the down-regulated ones, but no significant increase in the expression of heat shock genes were found [Lee et al., 2005]. However, the SAGE experiment was repeated only once and only one control with 2 h sham exposure was used. No confirmation experiment was reported to validate these differentially expressed genes.

Huang *et al.* investigated the effect of 1763 MHz RF EMF on gene expression in Jurkat cells by Applied Biosystems 1700 full genome expression microarray. The authors found that 68 genes were differentially expressed in the cells after exposure to RF EMF at SAR of 10 W/kg for 1 h and harvested immediately or after 5 h [Huang et al., 2006]. The authors repeated sets of experiment five times to collect biological triplicates in every sample but the differentially expressed genes were not confirmed by other methods.

Whitehead *et al.* have performed *in vitro* experiments with C3H 10T(1/2) mouse cells to determine whether Frequency Division Multiple Access (FDMA) or Code Division Multiple Access (CDMA) modulated RF radiations can induce changes in gene expression using the Affymetrix U74Av2 GeneChip. The GenesChip data showed the number of probe sets with an expression change greater than 1.3-fold was less than or equal to the expected number of false positives in C3H 10T(1/2) mouse cells after 835.62 MHz FDMA or 847.74 MHz CDMA modulated RF EMF exposure at SAR of 5 W/kg for 24 h. The authors concluded that the 24 h exposures to FDMA or CDMA RF radiation at 5 W/kg had no statistically significant effect on gene expression [Whitehead et al., 2006a; Whitehead et al., 2006b]. However, the authors did not demonstrate that these differentially expressed genes were real "false positive" with other methods.

In Gurisik's report, human neuroblastoma cells (SK-N-SH) were exposed to GSM 900 MHz RF signal at SAR of 0.2 W/kg for 2 h and recovered without field for 2 h post-exposure. Gene expression were examined by Affymetrix Human Focus Gene Arrays including 8400 genes and followed by real-time RT-PCR of the genes of interest. Only six genes were found to be slightly down-regulated in response to RF exposure comparing with mock-exposed cells. Furthermore, these genes can not be confirmed by real-time RT-PCR analysis. Thus, the authors concluded that the RF EMF exposure applied in this study could not change gene expression in SK-N-SH cells [Gurisik et al., 2006]. However, the array analysis experiment was repeated only once and only one array for exposure or sham exposure group.

Qutob *et al* have assessed the ability of exposure to a 1.9 GHz pulse-modulated RF field to affect global gene expression in U87MG glioblastoma cells by application of Agilent Human 1A (v1) oligonucleotide 22K microarray slides. The U87MG cells were exposed to 1.9 GHz pulse-modulated (50 Hz, 1/3 duty cycle) RF field at an average SAR of 0.1, 1.0 and 10.0 W/kg for 4 hours, and incubated for an additional 6 hours. The authors found no evidence that exposure to RF fields under different exposure conditions can affect gene expression in cultured U87MG cells. In this paper, the authors performed five experiments, each containing a single replicate and some of genes were confirmed as real "un-effected genes" [Qutob et al., 2006].

Zeng *et al.* have investigated gene expression profile in MCF-7 after exposing to GSM 1800 MHz RF EMF using Affymetrix Genechip U133A. The result showed that no gene with 100% consistency change were found in MCF-7 cells after intermittent exposure (5 min on/ 10 min off) to RF EMF at an average SAR of 2.0 W/kg for 24 h while five genes with 100% consistency change were found in MCF-7 at same exposure conditions but at SAR of 3.5 W/kg. However, these five differentially transcribed genes could not be further confirmed by real-time RT-PCR assay. Thus, this study did not provide evidence that RF EMF exposure can produce distinct effects on gene expression in the MCF-7 cells [Zeng et al., 2006].

Remondini *et al.* have investigated the effect of RF EMF on gene expression profile in six different cell lines or primary cells, and found various types of cell reacted differently in RF EMF exposure). RF EMF exposure changed gene expression in 900 MHz-exposed EA.hy926 endothelial cells (22 up-regulations, ten down-regulations), 900 MHz-exposed U937 lymphoblastoma cells (32 up-regulations, two down-regulations), and 1800 MHz-exposed HL-60 leukemia cells (11 up-regulations, one down-regulation) while NB69 neuroblastoma cells, T-lymphocytes, and CHME5 microglial cells did not show significant changes in gene expression. The authors concluded that there were alterations in gene expression in some human cells types exposed to RF-EMF but these chenges depended on the type of cells and RF-EMF signal [Remondini et al., 2006]. However, these RF responsive candidate genes in different types of cells were not confirmed yet.

Very recently, Zhao *et al.* have investigated the effects of RF EMF on gene expression of *in vitro* cultured rat neuron with Affymetrix Rat Neurobiology U34 array. Among 1200 candidate genes, 24 up-regulted genes and 10 down-regulated genes were identified after 24-h intermittent exposure (5 min on/ 10 min off) at an average SAR of 2.0 W/kg, which are associated with multiple cellular functions. The changes of most of genes were successfully validated by real-time RT-PCR, including genes involved in cytoskeleton, signal transduction pathway, metabolism [Zhao et al., 2007].

Belyaev et al. analyzed gene expression profile in RF exposed animals. Rats were exposed or sham exposed to GSM 915 MHz at whole body average SAR of 0.4 mW/g for 2 h and total RNA was extracted from cerebellum. Gene expression profiles were obtained by Affymetrix U34 GeneChips representing 8800 rat genes and analyzed with the Affymetrix Microarray Suite (MAS) 5.0 software. The results showed that 11 genes were up-regulated in a range of 1.34-2.74 folds and one gene was down-regulated 0.48-fold. The induced genes encode proteins with diverse functions including neurotransmitter regulation, blood-brain barrier (BBB), and melatonin production [Belyaev et al., 2006]. In this study, triplicate arrays were applied for three exposed samples or three sham exposed samples. But the differentially expressed genes were not confirmed by other methods.

III B . PROTEOMICS

Leszczynski *et al.* have provided perhaps some of the most relevant *in vitro* data by studying the effects of GSM 900 MHz RF EMF exposure [Leszczynski et al., 2002; Nylund and Leszczynski 2004; Nylund and Leszczynski 2006]. Firstly, the EA.hy926 cells were exposed to RF EMF at SAR of 2.0 W/kg over a one-hour period and the data indicated the RF exposure changed protein expression at a proteome scale, and up-regulated the level of HSP 27 protein and induced its hyper-phosphorylation. The activation of p38 mitogen activated kinase (MAPK) was partially responsible for the phosphorylation of the HSP. They confirmed HSP27 protein expression, phosphorylation and cellular distribution by independent protein analytical techniques including western blotting and indirect immunofluorescence [Leszczynski et al., 2002]. Secondly, the group screened 38 proteins with statistically significantly altered expression in the same cell line after GSM 900 MHz exposure at SAR of 2.4 W/kg for 1 h. An isoform of vimentin was confirmed as a responsive protein by Western blotting and indirect immunofluorescence. The authors concluded that the cytoskeleton might be one of the mobile phone radiation-responding cytoplasmic structures [Nylund and Leszczynski 2004]. Furthermore, they compared *in vitro* response to GSM 900 MHz RF EMF in EA.hy926 with its variant EA.hy926v1 by examination of protein expression using 2-DE. The results showed protein expression profiles were altered in both examined cell lines after RF EMF exposure. However, the affected proteins were differently in each of the cell lines, 38 and 45 differentially expressed proteins were found in EA.hy926 and EA.hy926v1 respectively. Several differentially expressed proteins in EA.hy926 cells were confirmed by other methods, but no differentially expressed protein in EA.hy926v1 cells was confirmed. Base on the transcriptome and proteome analysis data, the authors concluded that the response might be genome- and proteome-dependent [Nylund and Leszczynski 2006]. One thing should be mentioned that all the 2-DE analyses in Leszczynski group reports were replicated ten times.

Zeng *et al.* systematically explored the effects of 1800 MHz RF EMF on protein expression in MCF-7 cells by 2-DE, and revealed that a few but different proteins were differentially expressed under continuous or intermittent RF EMF exposure at SAR of 3.5 W/kg for 24 h or less, implying that the observed effects might have occurred by chance. By combination with the transcriptomics analysis data, this study did not provide convincing evidence that RF EMF exposure could produce distinct effects on gene and protein expression in the MCF-7 cells. The authors supposed that the MCF-7 cells may be less sensitive to RF EMF exposure [Zeng et al., 2006]. However, in this study, only triplicate gels were performed in each exposure condition experiment.

III C . SUMMARY

The effects of RF EMF on global gene and protein expression have been investigated in different biological systems, and most of studies were focused on the mobile phone utilization frequency (800-2000 MHz) at relative low exposure density (average SAR near 2.0 W/kg). Some studies reported negative results of RF EMF exposure on gene expression. For example, Whitehead *et al.* did not find differentially expressed genes in RF exposed C3H 10T(1/2) mouse cells [Whitehead et al., 2006a; Whitehead et al., 2006b]. Remondini *et al.* reported that NB69 cells, T lymphocytes, and CHME5 cells did not show significant changes in gene expression after RF EMF exposure [Remondini et al., 2006]. In Gurisik *et al.* [Gurisik et al., 2006]and Zeng *et al.* [Zeng et al., 2006]study, although they screened out several RF EMF-responsive candidate genes, they could not confirm these genes by real-time RT-PCR method.

Meanwhile, several groups claimed that RF EMF exposure can change gene and protein expression profile in certain types of cells and identified certain EMF responsive genes and proteins. Only one report found RF EMF exposure changed gene expression profile in neurons and most of changed genes were confirmed by real-time RT-PCR [Zhao et al 2007]. As to proteome analysis, only two groups have analyzed protein expression by proteomic approaches, including 2-DE and Mass Spectrum. Zeng *et al.* systematically explored the effects of 1800 MHz RF EMF on protein expression in MCF-7 cells by 2-DE, and revealed that a few but different proteins were differentially expressed under different exposure conditions, implying that the observed effects might have occurred by chance [Zeng et al., 2006]. However, in this study, only triplicate gels were performed in each exposure condition experiment. In contrast, Leszczynski group identified two RF EMF responsive proteins in EA.hy926 cells, i.e. HSP27 [Leszczynski et al., 2002] and vimentin [Leszczynski et al., 2004] with help of 2-DE and MS analysis. This group further confirmed the expression and cellular distribution of HSP27 and vimentin in RF exposed EA.hey926 cells by other methods including Western blotting and indirect immunofluorescence staining. Furthermore, they reported the changes of these RF EMF molecular targets had down-stream impact on cell physiology [Leszczynski et al., 2002; Leszczynski et al., 2004].

Generally, it seems that the response of a cell to RF EMF exposure depends on exposure condition, cell type, and/or the cell's genome- and proteome [[Remondini et al., 2006; Nylund and Leszczynski 2006].

IV. Overall Conclusion

Based on current available literature, it is justified to conclude that EMF exposure can change gene and/or protein expression in certain types of cells, even at intensities lower than ICNIRP recommended values. However, the biological consequences of most of the changed genes/proteins are still unclear, and need to be further explored. Thus, it is not the time point yet to assess the health impact of EMF based on the gene and protein expression data. The IEEE and WHO data bases do not include the majority of ELF studies; they do include the majority of the RF studies.

Currently, controversial data exist in the literature. The EMF research community should pay equal attention to the negative reports as to the positive ones. Not only the positive findings need to be replicated, all the negative ones are also needed to be validated.

It is noteworthy that low intensity EMF is a weak physical stimulus for a cell or organism, and high throughput screening techniques (HTSTs) would sacrifice its sensitivity to ensure its high throughput. It has been recognized there is methodological defects while analyzing weak effect with HTSTs, such as reproducibility and variability. Thus, more experimental replications are needed to reduce the ratio of noise over signal. Meanwhile, confirmation study must be included to assure the validity of the data.

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SECTION 6

EVIDENCE FOR GENOTOXIC EFFECTS
(RFR AND ELF Genotoxicity)

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TABLE OF CONTENTS

I. Introduction

Toxicity to the genome can lead to a change in cellular functions, cancer, and cell death. A large number of studies have been carried out to investigate the effects of electromagnetic field (EMF) exposure on DNA and chromosomal structures. The single-cell gel electrophoresis (comet assay) has been widely used to determine DNA damages: single and double strand breaks and cross-links. Studies have also been carried out to investigate chromosomal conformation and micronucleus formation in cells after exposure to EMF.

II. Radiofrequency radiation (RFR) and DNA damage *(28 total studies – 14 reported effects (50%) and 14 reported no significant effect (50%))*

II A. DNA studies that reported effects*:*

The following is a summary of the research data reported in the literature.

Aitken et al. [2005] exposed mice to 900-MHz RFR at a specific absorption rate (SAR) of 0.09 W/kg for 7 days at 12 h per day. DNA damage in caudal epididymal spermatozoa was assessed by quantitative PCR (QPCR) as well as alkaline and pulsed-field gel electrophoresis postexposure. Gel electrophoresis revealed no significant change in single- or double-DNA strand breakage in spermatozoa. However, QPCR revealed statistically significant damage to both the mitochondrial genome ($p < 0.05$) and the nuclear β-globin locus ($p < 0.01$).

Diem et al [2005] exposed human fibroblasts and rat granulosa cells to mobile phone signal (1800 MHz; SAR 1.2 or 2 W/kg; different modulations; during 4, 16 and 24 h; intermittent 5 min on/10min off or continuous). RFR exposure induced DNA single- and double-strand breaks as measured by the comet assay. Effects occurred after 16 h exposure in both cell types and after different mobile-phone modulations. The intermittent exposure showed a stronger effect in the than continuous exposure.

Gandhi and Anita [2005] reported increases in DNA strand breaks and micronucleation in lymphocytes obtained from cell phone users.

Garaj-Vrhovac et al [1990] reported changes in DNA synthesis and structure in Chinese hamster cells after various durations of exposure to 7.7 GHz field at 30 mW/cm^2.

Lai and Singh [1995; 1996; 1997a; 2005] and Lai et al. [1997] reported increases in single and double strand DNA breaks in brain cells of rats exposed for 2 hrs to 2450-MHz field at 0.6-1.2 W/kg.

Lixia et al. [2006] reported an increase in DNA damage in human lens epithelial cells at 0 and 30 min after 2 hrs of exposure to 1.8 GHz field at 3 W/kg.

Markova et al. [2005] reported that GSM signals affected chromatin conformation and gama-H2AX foci that colocalized in distinct foci with DNA double strand breaks in human lymphocytes.

Narasimhan and Huh [1991] reported changes in lambdaphage DNA suggesting single strand breaks and strand separation.

Nikolova et al. [2005] reported a low and transient increase in DNA double strand break in mouse embryonic stem cells after acute exposure to 1.7- GHz field.

Paulraj and Behari [2006] reported an increased in single strand breaks in brain cells of rats after 35 days of exposure to 2.45 and 16.5 GHz fields at 1 and 2.01 W/kg.

Phillips et al. [1998] found increase and decrease in DNA strand breaks in cells exposure to various forms of cell phone radiation.

Sun et al. [2006] reported an increase in DNA single strand breaks in human lens epithelial cells after 2 hrs of exposure to 1.8 GHz field at 3 and 4 W/kg. The DNA damages caused by 4 W/kg field were irreversible.

Zhang et al. [2002] reported that 2450-MHz field at 5 mW/cm^2 did not induce DNA and chromosome damage in human blood cells after 2 hrs of exposure, but could increase DNA damage effect induced by mitomycin-C.

Zhang et al. [2006] reported that 1800-MHz field at 3.0 W/kg induced DNA damage in Chinese hamster lung cells after 24 hrs of exposure.

II B. DNA studies that reported no significant effect:

Chang et al. [2005] using the Ames assay found no significant change in mutation frequency in bacteria exposed for 48 hrs at 4W/kg to an 835-MHz CDMA signal.

Hook et al. [2004] showed that 24-hr exposure of Molt-4 cells to CDMA, FDMA, iDEN or TDMA modulated RF radiation did not significantly alter the level of DNA damage.

Lagroye et al. [2004a] reported no significant change in DNA strand breaks in brain cells of rats exposed for 2 hrs to 2450-MHz field at 1.2 W/kg.

Lagroye et al. [2004b] found no significant increases in DNA-DNA and DNA-protein cross-link in C3H10T(1/2) cells after a 2-hr exposure to CW 2450 MHz field at 1.9 W/kg.

Li et al. [2001] reported no significant change in DNA strand breaks in murine C3H10T(1/2) fibroblasts after 2 hrs of exposure to 847.74 and 835.02 MHz fields at 3-5 W/kg.

Maes et al. [1993, 1996, 1997, 2000, 2001, 2006] published a series of papers on in vitro genotoxic effects of radiofrequency radiation and interaction with chemicals. Their mostly found no significant effect.

Malyapa et al. [1997a,b, 1998] reported no significant change in DNA strand-breaks in cells exposed to 2450-Hz and various forms of cell phone radiation. Both in vitro and in vivo experiments were carried out.

McNamee et al. [2002a,b, 2003] found no significant increase in DNA breaks and micronucleus formation in human leukocytes exposed for 2 hrs to 1.9 GHz field at SAR up to 10 W/kg.

Sakuma et al. [2006] exposed human glioblastoma A172 cells and normal human IMR-90 fibroblasts from fetal lungs to mobile communication radiation for 2 and 24 hrs. No significant change in DNA strand breaks were observed up to 800 mW/kg.

Stronati et al. [2006] showed that 24 hrs of exposure to 935-MHz GSM basic signal at 1 or 2 W/Kg did not cause DNA strand breaks in human blood cells.

Tice et al. [2002] measured DNA single strand breaks in human leukocytes using the comet assay after exposure to various forms of cell phone signals. Cells were exposed at 37±1°C, for 3 or 24 h at average specific absorption rates (SARs) of 1.0-10.0 W/kg. Exposure for either 3 or 24 h did not induce a significant increase in DNA damage in leukocytes.

Vershaeve et al. [2006] long-term exposure (2 hrs/day, 5 days/week for 2 years) of rats to 900 MHz GSM signal at 0.3 and 0.9 W/kg did not significantly affect levels of DNA strand breaks in cells.

Vijayalaximi et al [2000] reported no significant increase in single strand breaks in human lymphocytes after 2 hrs of exposure to 2450-MHz field at 2 W/kg.

Zeni et al. [2005] reported that a 2-hr exposure to 900-MHz GSM signal at 0.3 and 1 W/kg did not significantly affect levels of DNA strand breaks in human leukocytes.

III. Micronucleus studies (29 Total studies: 16 reported effects (55%) and 13 reported no significant effect (45%))

III A. Micronucleus studies that reported effects:

Balode [1996] obtained blood samples from female Latvian Brown cows from a farm close to and in front of the Skrunda Radar and from cows in a control area. Micronuclei in peripheral erythrocytes were significantly higher in the exposed cows.

Busljeta et al. [2004] exposed male rats to 2.45 GHz RFR fields for 2 hours daily, 7 days a week, at 5-10 mW/cm^2 for up to 30 days. Erythrocyte count, haemoglobin and haematocrit were increased in peripheral blood on irradiation days 8 and 15. Anuclear cells and erythropoietic precursor cells were significantly decreased in the bone marrow on day 15, but micronucleated cells were increased.

D'Ambrosio et al. [2002] exposed human peripheral blood to 1.748 GHz continuous wave (CW) or phase-modulated wave (GMSK) for 15 min at a maximum specific absorption rate of ~5 W/kg. No changes were found in cell proliferation kinetics after exposure to either CW or GMSK fields. Micronucleus frequency result was not affected by CW exposure but a statistically significant increase in micronucleus was found following GMSK exposure.

Ferreira et al. [2006] found that rat offspring exposed to radiation from a cellular phone during their embryogenesis showed a significant increase in micronucleus frequency.

Fucic et al. [1992] reported increase in frequencies of micronuclei in the lymphocytes of humans exposed to microwaves.

Gandhi and Singh [2005] analyzed short term peripheral lymphocyte cultures for chromosomal aberrations and the buccal mucosal cells for micronuclei. They reported an increase in the number of micronucleated buccal cells and cytological abnormalities in cultured lymphocytes.

Garaj-Vrhovac et al [1992] exposed human whole-blood samples to continuous-wave 7.7 GHz radiation at power density of 0.5, 10 and 30 mW/cm^2 for 10, 30 and 60 min. In all experimental conditions, the frequencies of all types of chromosomal aberrations (dicentric and ring chromosomes) and micronucleus were significantly higher than in the control samples.

Garaj-Vrhovac et al. [1999] investigated peripheral blood lymphocytes of 12 subjects occupationally exposed to microwave radiation. Results showed an increase in frequency of micronuclei as well as disturbances in the distribution of cells over the first, second and third mitotic division in exposed subjects compared to controls.

Haider et al. [1994] exposed plant cuttings bearing young flower buds for 30 h on both sides of a slewable curtain antenna (300/500 kW, 40-170 V/m) and 15 m (90 V/m) and 30 m (70 V/m) distant from a vertical cage antenna (100 kW) as well as at the neighbors living near the broadcasting station (200 m, 1-3 V/m). Laboratory controls were maintained for comparison. Higher micronucleus frequencies than in laboratory controls were found for all exposure sites in the immediate vicinity of the antennae,

Tice et al. [2002] measured micronucleus frequency in human leukocytes using the comet assay after exposure to various forms of cell phone signals. Cells were exposed at 37±1°C, for 3 or 24 h at average specific absorption rates (SARs) of 1.0-10.0 W/kg. Exposure for 3 h did not induce a significant increase in micronucleated lymphocytes. However, exposure to each of the signals for 24 h at an average SAR of 5.0 or 10.0 W/kg resulted in a significant and reproducible increase in the frequency of micronucleated lymphocytes. The magnitude of the response (approximately four fold) was independent of the technology, the presence or absence of voice modulation, and the frequency.

Trosic et al. [2001] investigated the effect of a 2450-MHz microwave irradiation on alveolar macrophage kinetics and formation of multinucleated giant cells after whole body irradiation of rats at 5-15 mW/cm^2. A group of experimental animals was divided in four subgroups that received 2, 8, 13 and 22 irradiation treatments of two hours each. The animals were killed on experimental days 1, 8, 16, and 30. Multinucleated cells were significantly increased in treated animals. The increase in number of nuclei per cell was time- and dose-dependent. Macrophages with two nucleoli were more common in animals treated twice or eight times. Polynucleation was frequently observed after 13 or 22 treatments.

Trosic et al. [2002] exposed adult male Wistar for 2 h a day, 7 days a week for up to 30 days to continuous 2450-MHz microwaves at a power density of 5-10mW/cm^2. Frequency of micronuclei in polychromatic erythrocytes showed a significant increase in the exposed animals after 2, 8 and 15 days of exposure compared to sham-exposed control.

Trosic et al. [2004] investigated micronucleus frequency in bone marrow red cells of rats exposed to a 2450-MHz continuous–wave microwaves for 2 h daily, 7 days a week, at a power density of 5-10 mW/cm^2 (whole body SAR 1.25 +/- 0.36 (SE) W/kg). The frequency of micronucleated polychromatic erythrocytes was significantly increased on experimental day 15.

Trosic et al. [2006] exposed rats 2 h/day, 7 days/week to 2450-MHz microwaves at a whole-body SAR of 1.25 +/- 0.36W/kg. Control animals were included in the study. Bone marrow micronucleus frequency was increased on experimental day 15, and

7) To identify “next steps” in advancing biologically-based exposure standards that are protective of public health; that are derived in traditional public health approaches.

Eleven (11) chapters documenting key scientific studies and reviews that identify low-intensity effects of electromagnetic fields have been produced by the members of the BioInitiative Working Group; four additional chapters are provided that discuss public health considerations, how the scientific information should be evaluated in the context of prudent public health policy, and discussing the basis for taking precautionary and preventative actions that are proportionate to the knowledge at hand. Other scientific review bodies and agencies have reached different conclusions by adopting standards of evidence so unreasonably high as to exclude any finding of scientific concern, and thus justify retaining outdated thermal standards. The clear consensus of the BioInitiative Working Group members is that the existing public safety limits are inadequate. New approaches to development of public safety standards are needed based on biologically-based effects, rather than based solely on RF heating (or induced currents in the case of ELF). The Report concludes with recommended actions that are proportionate to the evidence and in accord with prudent public health policy.

The Report also presents information about what level of scientific evidence is sufficient to make changes now. It addresses the questions:

- What is “proof”? Do we need proof before we take any action? Is an unreasonably high and overly-restrictive definition of “proof” what is keeping some governments from facing the evidence that the need for new public exposure limits is demonstrated?
- What is sufficient evidence? How much evidence is needed? Do we have it yet?
- Do scientists and public health experts differ on when action is warranted? If so, how?
- What is the prudent course of action when the consequence of doing nothing is likely to have serious global consequences on public health, confidence in governments and social/economic resources?
- What are the costs of guessing wrong and under-reacting? Or, of over-reacting?
- Whose opinions should count in the process of deciding about health risks and harm?
- Is the global, governmental process addressing these questions transparent and responsive to public concerns? Or, is it a cosmetic process giving the illusion of transparency and democratic participation? Are some countries ostracized for views

and actions that are more protective of public health? How can we equitably decide on the appropriate level of public protection within each country, when it is obvious that some countries would be best off spending their time and money on basic medical needs and infrastructure improvements to save lives, when others need to look at prevailing disease endpoints relevant to their populations, and wish to act accordingly?

- How has the effort for global harmonization of ELF and RF exposure standards thwarted the efforts of individual countries to read, reason and choose?
- How much control have special interests exerted over harmonization goals and safety standards? How much over scientific funding, research design, dissemination of research results and media control? Are the interests of the public being conserved?
- What actions are proportionate to the knowledge we now have? What is preventative action and how does it differ from precautionary action?

It describes what the existing exposure standards are, and how some international governmental bodies are standing by the old exposure standards despite evidence that change is needed.

A good way to compare what kind of actions should be taken now is to look at what has been done with other environmental toxicants. It is well-established that public health decision-makers should act before it is too late to prevent damage that can reasonably be expected now; especially where the harm may be serious and widespread. Some actions that can prevent future harm are identified. The basis for taking action now rather than later is explained. This report can serve as a basis for arguing the scientific and public health policy reasons that changes are needed. It documents information for decision-makers and the public who want to understand what is already known biological effects occuring at low-intensity exposures; and why it is reasonable to expect our governmental agencies to develop new, biologically-based exposure standards that protect the public.

Problems with Existing Public Health Standards (Safety Limits)

Today's public exposure limits are based on the presumption that heating is the only concern when living organisms are exposed to RF and ELF. These exposures can create tissue heating that is well known to be harmful in even very short-term doses. As such, thermal limits do serve a purpose. For example, for people whose occupations require them to work around electrical power lines or heat-sealers, or for people who install and service wireless antenna towers; thermally-based limits are necessary to prevent damage from heating (or, in the case of ELF -

from induced currents in tissues). In the past, scientists and engineers developed exposure standards for electromagnetic radiation based what we now believe are faulty assumptions that the right way to measure how much non-ionizing energy humans can tolerate (how much exposure) without harm is to measure only the heating of tissue (for – induced currents in the body). In the last few decades, it has been established beyond any reasonable doubt that bioeffects and some adverse health effects occur at far lower levels of RF and exposure where no heating occurs at all; some effects are shown to occur at several hundred thousand times below the existing public safety limits where heating is an impossibility. Effects occur at non-thermal or low-intensity exposure levels far below the levels that federal agencies say should keep the public safe. For many new devices operating with wireless technologies, the devices are exempt from any regulatory standards. The existing standards have been proven to be inadequate to control against harm from low-intensity, chronic exposures, based on any reasonable, independent assessment of the scientific literature. It means that an entirely new basis (a biological basis) for new exposure standards is needed. New standards need to take into account what we have learned about the effects of non-ionizing electromagnetic fields and to design new limits based on biologically-demonstrated effects that are important to proper biological function in living organisms. It is vital to do so because the explosion of new sources has created unprecedented levels of artificial electromagnetic fields that now cover all but remote areas of the habitable space on earth. Mid-course corrections are needed in the way we accept, test and deploy new technologies that expose us to ELF and RF in order to avert public health problems of a global nature.

At least three decades of scientific study and observation of effects on humans and animals shows that non-thermal exposure levels can result in biologically-relevant effects. There should be no effects occurring at all. Yet, clearly they do occur. This means the standards for protecting public health are based on the wrong premise - that only what heats tissue can result in harm. It does appear that it is the INFORMATION conveyed by electromagnetic radiation, rather than the heat, which causes biological changes, some of which may lead to unwellness, illness and even death, According to Adey (2004):

> *"There are major unanswered questions about possible health risks that may arise from human exposures to various man-made electromagnetic fields where these exposures are intermittent, recurrent, and may extend over a significant portion of the lifetime of an*